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| EXAMINER | |
|---|---|
| KISHORE, G | |
| **ART UNIT** | **PAPER NUMBER** |
| 1615 | 6 |

**DATE MAILED:** 07/09/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 4-15-99

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) 8, 9 & 11-19 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 8, 9 & 11-19 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

## DETAILED ACTION

**The request for the corrected filing receipt dated 12-21-98 and the amendment dated 4-15-99 are acknowledged.**

**Claims included in the prosecution are 8-9 and 11-19.**

### *Claim Rejections - 35 U.S.C. § 112*

**1. The following is a quotation of the second paragraph of 35 U.S.C. 112:**

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

**2. Claims 13-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

**The method claim is still deemed to be indefinite since it fails to recite the method of preparation steps; applicant's amendment to introduce 'entrapping' does not overcome this rejection since a method of preparation claim should recite how the compound is entrapped.**

### *Double Patenting*

**3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the**

**unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).**

**A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).**

**Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).**

**4. Claims 8-9, 11-12, 14-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,013,556. Although the conflicting claims are not identical, they are not patentably distinct from each other because the generic hydrophilic polymer encompasses PEG in the claims of said patent.**

**Applicant's arguments have been fully considered, but are not found to be persuasive. With regard to composition claims, instant claims and the patented claims recited the same composition; reciting the intended use does not change the nature of the composition already patented. With regard to the method claims, both the claims in the patent and present application are drawn to the same composition and the same mode of administration, i.e., intravenous injection and for the treatment of tumors (see claim 29 of the patent which is drawn to the site (tumor) specific delivery of the anti-tumor agent) and therefore, the method of localization at the tumor infected site is implicit.**

**5. Claims 8-9, 11-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 5,213,804. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant generic 'hydrophilic polymer' encompasses the specific polymers in the claims of said patent.**

**Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants' argue that 804 is drawn to a method of treatment of solid tumors and the claims in said patent do not suggest the liposomes are able to accumulate at the site of infected tissue. This argument is not found to be persuasive. With regard to composition claims, instant claims and the patented claims recited the same composition; reciting the intended use does not change the nature of the composition already patented. With regard to the method claims in the patent:- they are drawn to the treatment of animals infected with tumors and therefore, site specific delivery is implicit.**

*Claim Rejections - 35 U.S.C. § 102*

**6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:**

**A person shall be entitled to a patent unless --**

**(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

**7. Claims 8-9 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Sears (EP 0 118 316).**

**Sears discloses synthetic lipids formed by reacting phosphatidylethanolamine and polyethylene glycol. This amphiphilic compound is used to encapsulate drugs. The method of encapsulation involves the evaporation to dryness of said synthetic lipid and hydrating it with an aqueous medium and vortexed (note the abstract, columns 2-5, Examples 10-14). Instant 'therapeutic compound active against the pathogen causing the infection' is deemed be included in 'drug' taught by Sears.**

**Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants argue that Applicant argues that Sears' structures are not liposomes. The method of preparation of Sears involves the evaporation of the amphipathic lipid in an organic solvent and then hydrating the lipid with an aqueous medium. This is a classical method of preparation of liposomes and the same as in instant invention. The product therefore, is the same as in instant invention. There are numerous articles in literature on the preparation of liposomes using this classical technique and the examiner cites the review article by Deamer as evidence. The examiner al so cites applicants' own prior patent dealing with the preparation of PEG-liposomes using the same methodology (note col. 19, line 10 et seq of US 5,013,556; see also**

**instant specification on**

**page 58). Furthermore, contrary to applicant's arguments there is no clear evidence in Sear s that the structures are not liposomes. It is the interpretation of the examiner that Sears m erely distinguishes his structures which have PEG linked phospholipid (liposomes) from cla ssical liposomes which do not have PEG linked phospholipid. Applicant's arguments thus, are not found to be persuasive.**

*Claim Rejections - 35 U.S.C. § 103*

**8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:**

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

**9. Claims 8-9 and 11-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sears (EP 0 118 316).**

**Sears discloses synthetic lipids formed by reacting phosphatidylethanolamine and polyethylene glycol. This amphiphilic compound is used to encapsulate drugs. The method of encapsulation involves the evaporation to dryness of said synthetic lipid and hydrating it with an aqueous medium and vortexed (note the abstract, columns 2-5, Examples 10-14). Although Sears does not teach instant drugs and instant polymers, it is deemed to be within**

**the skill of the art to encapsulate any drug or use similar hydrophilic polymers with the expectation of obtaining similar results.**

**Applicants' arguments are similar to their arguments regarding the 102 rejection which have been addressed above.**

**10. Claims 8-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janoff ((4,897,384) or Popescu (4,981,692) in view of Yoshioka (5,593,622).**

**Janoff teaches gentamycin containing liposomes (note the abstract, examples and claims). Janoff however, does not teach that the phospholipids used in the formation of liposomes be attached with the hydrophilic polymer such as polyethylene glycol (PEG).**

**As pointed out above, Popescu teaches liposome formulations containing gentamycin. Popescu although teaches that cholesterol-PEG could be used in the liposomes, does not teach that phospholipids used in the formation of liposomes be attached with the hydrophilic polymer, polyethylene glycol (PEG).**

**Yoshioka teaches that when phospholipids which are attached to PEG are used in the formation of liposomes, the hydrophilic moiety of PEG prevents the adsorption of plasma proteins on the liposomes and the subsequent agglutination of liposomes (note the abstract). In essence Yoshioka indirectly teaches that the stability of the liposomes is increased.**

**The attachment of PEG to the surface of the liposomes (by coupling with the phospholipid) taught by Janoff or Popescu would have been obvious to one of ordinary skill**

**in the art because PEG prevents the adsorption of plasma proteins on the liposomes and the subsequent agglutination of liposomes as taught by Yoshioka.**

**Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants argue that the important feature of the Janoff preparation appears to be the ability of the selected ligand to competitively bind with the toxicity receptor and that the modification of the phospholipid head group with a PEG chain is nowhere suggested in Janoff. This argument is not found to be persuasive since this rejection is on the combination of Janoff with Yoshioka and one skilled in the art would be motivated to couple PEG based on the teachings of Yoshioka. With regard to applicants' arguments that a modification of Janoff's preparation would likely alter its ability to competitively bind and reduce toxicity, the examiner points out that this argument is without any data and therefore, deemed to be speculative in nature.**

**Applicants' arguments that Popescu is concerned with RES are not found to be persuasive. On columns 4 and 5 Popescu only refers to the sites the bacteria is likely to infect. On column 5, Popescu teaches the same listeria which is listed in instant specification as one of the bacteria treatable by instant composition (page 42). Since the bacteria are the same the sites of the infection are the same.**

**11. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).**

**A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.**

**12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.**

**The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.**

**If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.**

**Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].**

**All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility**

**that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.**

**Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.**

**Gollamudi S. Kishore, Ph. D**

**Primary Examiner**

**Group 1600**

***gsk***

**July 2, 1999**